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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,380	04/18/2000	Donald Choy Chang	MLY-5	2514

7590

04/22/2003

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.  
**09/551,380**

Applicant(s)  
**Chang et al.**

Examiner  
**Christian L. Fronda**

Art Unit  
**1652**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 25, 26, 28, 30-34, and 36 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 25, 26, 28, 30-34, and 36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/30/2003 (Paper No. 19) has been entered.
2. In the AMENDMENT A dated 10/30/2002 (Paper No. 16), Applicants have canceled claims 29, 35, and 37-39 and amended claims 1, 3, 4, 5, 6, 28, and 36.
3. Claims 1-7, 25, 26, 28, 30-34, and 36 are under consideration in this Office Action.

### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 1-7, 25, 26, 28, 30-34, and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a green fluorescent protein (GFP) having a protease cleavage site and an amino acid sequence consisting of SEQ ID NO: 41; does not reasonably provide enablement for any fluorescent protein "comprising an 11-stranded  $\beta$ -barrel formed from 11  $\beta$ -sheets surrounding a chromophore-containing co-axial  $\alpha$ -helix, each of said  $\beta$ -sheets forming said  $\beta$ -barrel joined by a loop structure to at least one other adjacent  $\beta$ -sheet forming said  $\beta$ -barrel". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.  
The claimed invention requires the crystal structure of any fluorescent protein in order to identify, determine the number, and position of any  $\beta$ -sheet structure. While molecular biological techniques and several crystallization methods for proteins are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific fluorescent protein and how to obtain a suitable crystal for structure determination by X-ray is lacking.

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Thus, searching for any fluorescent protein and for crystallization conditions to obtain an adequate crystal of any fluorescent protein for structure determination by x-ray diffraction method is well outside the realm of routine experimentation and predictability in the art of success is extremely low, see Branden et al. page 271 cited in the previous Office Action dated 10/24/2001 (Paper No. 10).

The conditions of crystallization is highly dependent on the fluorescent protein itself and any minor change in the amino acid sequence may require search for new crystallization conditions. The amount of experimentation to identify the specific fluorescent protein and conditions to grow a single crystal suitable for structure determination in order to identify, determine the number, and position of any  $\beta$ -sheet structure is enormous. Since routine experimentation in the art does not include screening for vast numbers of fluorescent proteins and crystallization conditions where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact fluorescent protein to be crystallized and the conditions under which the fluorescent protein would crystallize and produce an adequate crystal for structural determination by X-ray. Without such a guidance, the experimentation left to those skilled in the art is undue.

### ***Claim Rejections - 35 U.S.C. § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 25, 26, 28, 29, and 34 stand rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. This reference was attached to the previous Office Action dated 10/24/2001 (Paper No. 10).

Applicant's arguments filed 10/30/2002 (Paper No. 16) have been fully considered but they are not persuasive. Applicant's argue that the claimed invention is directed to an inserted cleavage site within a single fluorescent protein molecule. However, the claims do not recite the limitations that the claimed protein is a single fluorescent protein molecule and the claimed insertion site is not used to link two different fluorescent protein molecules. Thus, the reference teachings Xu et al. anticipate the claimed invention.


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***Conclusion***

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

  
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SUPERVISORY PATENT EXAMINER  
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